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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/817,248	04/02/2004	Sherin S. Abdel-Meguid	50201/003002	3934

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EXAMINER	
KOSAR, ANDREW D	

ART UNIT	PAPER NUMBER
1654	

DATE MAILED: 05/17/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/817,248	ABDEL-MEGUID ET AL.	
	Examiner	Art Unit	
	Andrew D. Kosar	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-103 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) 1-103 are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-103 are pending and require restriction to one of the following inventions.

Election/Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-33, drawn to compounds of formula (I), classified in class 530, subclass 300.

II. Claims 34-36, drawn to a method of treating a thromboembolic disorder with a compound of formula (I), classified in class 514, subclass 2.

III. Claim 37-54, drawn to compounds of formula (II), classified in class 568, subclass 328.

IV. Claims 55-57, drawn to a method of treating a thromboembolic disorder with a compound of formula (II), classified in class 514, subclass 481.

V. Claims 58-60, drawn to a computer with atomic coordinates, classified in class 345, subclass 418.

VI. Claims 61-66, drawn to a method of designing or selecting Factor XIa ligands, classified in class 436, subclass 501.

VII. Claims 67-78, drawn to a method of manufacturing a Factor XIa ligand, classified in class 530, subclass 345.

VIII. Claims 79-90, drawn to a method for evaluating a Factor XIa catalytic domain ligand, classified in class 435, subclass 70.1.

IX. Claim 91, drawn to a crystal of Factor XI, classified in class 530, subclass 384.

X. Claim 92, drawn to a method of generating a homology model of Factor XI catalytic domain of interest, classified in class 434, subclass 277.

XI. Claim 93, drawn to a method of determining the 3D structure of Factor XI catalytic domain of interest by crystal diffraction, classified in class 117, subclass 14.

XII. Claims 94, drawn to SEQ ID NO: 1 (human FXIa) classified in class 530, subclass 350.

XIII. Claim 96, drawn to SEQ ID NO: 2 (Rabbit FXIa) classified in class 530, subclass 350.

XIV. Claim 98, drawn to SEQ ID NO: 3 (mouse FXIa) classified in class 530, subclass 350.

XV. Claim 95, drawn to DNA encoding SEQ ID NO: 1, classified in class 536, subclass 23.1.

XVI. Claim 97, drawn to DNA encoding SEQ ID NO: 2, classified in class 536, subclass 23.1.

XVII. Claims 99, drawn to DNA encoding SEQ ID NO: 3, classified in class 536, subclass 23.1.

XVIII. Claim 98, drawn to SEQ ID NO:4 (rat FXIa), classified in class 530, subclass 350.

XIX. Claim 99, drawn to DNA encoding SEQ ID NO:4, classified in class 536, subclass 23.1.

XX. Claims 100 and 102, drawn to a purified mutant Factor XI protein, classified in class 530, subclass 350.

XXI. Claims 101 and 103, drawn to DNA encoding the mutant Factor XI protein, classified in class 536, subclass 23.1.

Claims 98 and 99 link(s) inventions XIV, and XVII-XIX. The restriction requirement between the linked inventions is subject to the nonallowance of the linking claim(s), claims 98 and 99. Upon the allowance of the linking claim(s), the restriction requirement as to the linked inventions shall be withdrawn and any claim(s) depending from or otherwise including all the limitations of the allowable linking claim(s) will be entitled to examination in the instant application. Applicant(s) are advised that if any such claim(s) depending from or including all the limitations of the allowable linking claim(s) is/are presented in a continuation or divisional application, the claims of the continuation or divisional application may be subject to provisional statutory and/or nonstatutory double patenting rejections over the claims of the instant application. Where a restriction requirement is withdrawn, the provisions of 35 U.S.C. 121 are no longer applicable. *In re Ziegler*, 44 F.2d 1211, 1215, 170 USPQ 129, 131-32 (CCPA 1971). See also MPEP § 804.01.

The inventions are distinct, each from the other because of the following reasons:

Inventions **I and III, IX, and XII-XI** are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are drawn to different compounds with different structures and would be expected to have different modes of action. Compounds of Formula (I) are peptidic, while the compounds of Formula (II) are bicyclic, quinoline-like, or naphthyl-like ring structures; further, Group IX is a crystal of Factor XI, Groups XII-XIV are SEQ ID NOs:1-3,

Groups XVIII is SEQ ID NO:4, Group XX is a mutant Factor XI protein. SEQ ID NOs: 1-4 each come from a different species source, and have different sequences. Groups XV-XVIII, XIX, and XXI are each drawn to DNA/polynucleotides encoding proteins, which are structurally distinct from the proteins, themselves, and from the inventions of the other Groups, each encoding a different protein. DNA has a distinctly different mode of action from proteins, and is not usable with a protein, or a crystal of a protein.

Inventions **I-IV and V-XXI** are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions the inventions of Groups V-XVII do not require the products, or methods, of Groups I-IV, and they are not disclosed as being capable of use together, and have different functions. The methods of Groups II and IV are treating, while the methods of the other groups are for designing and/or screening compounds with a receptor. Further, Groups V-VIII and XII-XIX are drawn to Factor XIa, while, inventions IX-XI, XX, and XXI are drawn to Factor XI, not Factor XIa.

Inventions **I and II** are related as product and process of use; and inventions **III and IV** are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case one could treat thromboembolic disorders with either the compound of Formula (I) or the compound

of Formula (II), two structurally distinct compounds. Further one could treat a thromboembolic disorder with heparin, dipyridamole, ticlopidine, wafarin, or enoxaparin.

Inventions **V and VI-VIII** are related as process and apparatus for its practice. The inventions are distinct if it can be shown that either: (1) the process as claimed can be practiced by another materially different apparatus or by hand, or (2) the apparatus as claimed can be used to practice another and materially different process. (MPEP § 806.05(e)). In this case the apparatus, a computer, can be used for basic word-processing or reading e-mail.

Inventions **VI-VIII** are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions have different steps (modes of operation/functions), and the methods have different results (effects), and are not capable of use together.

Inventions **IX-XI** are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions are not capable of use together and have different modes of operation. The crystal of Group IX is not required for the methods of Groups X or XI. Additionally, the method of Group X is computationally generated using homology software (e.g., using Insight II, or related software packages), while the method of Group XI requires obtaining crystal data and generation of an electron density map.

The search for each of the above inventions is not co-extensive particularly with regard to the non-patented literature search. A reference which would anticipate the invention of one

group would not necessarily anticipate or even make obvious another group. For example, a search of the literature regarding Formula (I) would not necessarily lead to the discovery of all pertinent literature with regards to a computer with atomic coordinates store therein.

Additionally, the compounds of the instant application are distinct, absent evidence to the contrary, and would require a unique search strategy. The search for the distinct compounds is conducted based on their chemical structure or sequence. Therefore, the search of one chemical structure would not necessarily lead to the discovery of another structure, nor would it necessarily lead to the discovery of methods of using and/or making.

Because these inventions are distinct for the reasons given above, have acquired a separate status in the art as shown by their different classification, and the search for one invention would not necessarily lead to the discovery of another invention, restriction for examination purposes as indicated is proper, and to not restrict would be an undue burden on the Examiner.

With regards to Groups I/II: Claims 1-36 generic to a plurality of disclosed patentably distinct species comprising Compounds of Formula (I).

With regards to Groups III/IV: Claims 1-36 generic to a plurality of disclosed patentably distinct species comprising Compounds of Formula (II).

Commensurate with election of any of Groups I-IV, Applicant is required under 35 U.S.C. 121 to elect a single disclosed species, even though this requirement is traversed.

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the

examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

In order to effect a complete response to this requirement, Applicant is required to identify the compound (e.g., Compound 5, table 3a), and/or each variable moiety specifically [e.g., for Group I/II, R1 is Cl-Trp (last structure), b = 1, R 3, R2 are each H, R1 is NH2, A is R8-AA2, where R8 is C2-7 acyl, AA2 is a bond, m is 1 and R0 is C1-6 alkylamino], as it would be an undue burden to search the myriad of compounds embraced by the generic.

This application contains claims directed to the following patentably distinct species of the claimed invention: In Groups II and IV, claims 36 and 57 each recite 24 distinct thromboembolic disorders, each with a different etiology and patient population, thus requiring a different search.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable. Currently, in Group II, claims 34 and 35 are generic, and in Group IV, claims 55 and 56 are generic.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the

examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Rejoinder Practice

The Examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and a product claim is subsequently found allowable, withdrawn process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined in accordance with the provisions of MPEP § 821.04. **Process claims that depend from or otherwise include all the limitations of the patentable product** will be entered as a matter of right if the amendment is presented prior to final rejection or allowance, whichever is earlier. Amendments submitted after final rejection are governed by 37 CFR 1.116; amendments submitted after allowance are governed by 37 CFR 1.312.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.** Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Andrew D. Kosar whose telephone number is (571)272-0913. The examiner can normally be reached on Monday - Friday 8am-430pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Bruce Campell can be reached on (571)272-0974. The fax phone number for the organization where this application or proceeding is assigned is (571)273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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